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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,957	01/09/2002	Peter John Meikle	TLHR-0005	2903
7590 07/05/2005			EXAMINER	
Jackson Walker LLP 2435 N. Central Expressway Suite 600 Richardson, TX 75080			LAM, ANN Y	
			ART UNIT	PAPER NUMBER
			1641	

DATE MAILED: 07/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/936,957

Applicant(s)

MEIKLE ET AL.

Examiner

Ann Y. Lam

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 04 April 2005.  
2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.  
3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-20 and 36 is/are pending in the application.  
4a) Of the above claim(s) 21-35, 37 and 38 is/are withdrawn from consideration.  
5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.  
6) ☒ Claim(s) 1-20 and 36 is/are rejected.  
7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.  
8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.  
10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)  
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)  
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.  
4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.  
5) ☐ Notice of Informal Patent Application (PTO-152)  
6) ☐ Other: \_\_\_\_\_

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## **DETAILED ACTION**

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 18 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 18, line 3, recites the limitation "and subset thereof". There is not support in the original specification for a definition of a subset of lysosomal storage disorders listed in claim 18. Nor is it clear as to what "subset" means (a combination of the diseases listed in claim 18 or what else?) (The specification discloses that an elevated level of saposin correlates with the presence of several lysosomal storage disorders (page 6, lines 8-9). However, this disclosure does not describe more than one lysosomal storage disorder being diagnosed in a single assay.)

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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Claims 1-20 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague because it is not clear as to what level of saposin indicates the presence of the lysosomal storage disorder. The claim is also not clear as to what levels of saposin are involved in the monitoring of the lysosomal storage disorder. The claim is also not clear as to what level of saposin and/or which saposin is correlated to each of the lysosomal storage disorders. Page 4 of the specification indicates there are 30 lysosomal disorders and page 5 of the specification indicates there are 4 saposins. The detection of which saposin and at which level is indicative of the presence of which of the 30 possible lysosomal disorders? Applicant has not indicated which specific lysosomal disorder, nor a specific level of saposin or a specific level of increase or specific level of decrease level of saposin indicates the presence of the specific disease. In line 6, the recitation of "similar or different" is vague and indefinite as to what level of saposin is determined. (For example, if "different" indicates a lysosomal storage disorder, then does "different" mean lower or higher or both, at how much lower or higher and which lysosomal disorder does it indicate?)

Claim 7 is also indefinite because it is not clear what this comparison determines. Does it indicate the presence of the disorder (and which specific disorder)?

Claims 11 and 12 are vague because it is not clear as to what level of saposin, or a specific level of increase or decrease of saposin, indicates progression of the disorder. The claim is also not clear as to which of the 30 possible lysosomal disorders

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is being referred to relative to the 4 possible saposins that are being measured. (A list of saposin levels correlating to certain lysosomal storage disorders does not indicate a *progression* of a disorder.)

Claim 13 is vague because the recitation of "the second saposin" lacks antecedent support. The claim is further vague because it does not further limit claim 1. Claim 1 already recites the saposins in claim 13.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

1. Claims 1-4, 7, 8, 13-15, 17 and 18 rejected under 35 U.S.C. 103(a) as being unpatentable over O'Brien et al. (1991) Saposin proteins: structure, function, and role in human lysosomal disorders, THE FASEB JOURNAL, vol. 5(3), 301-8, in view of Sano et al., "Sphingolipid hydrolase activator proteins and their precursors", Biochemical and biophysical research communications, 165 (3), pp. 1191-7, 1989.

O'Brien teaches the invention substantially as claimed. More specifically, as to claim 1, O'Brien discloses the method of monitoring a lysosomal storage disorder in a

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patient (page 306, right column, lines 21-22), comprising: measuring the level of at least one saposin in a tissue sample of the patient (page 306, right column, lines 17-19),

comparing the first level to a baseline level, wherein the baseline level is determined in a control population of patients unaffected by the lysosomal storage disorder (see page 307, description of figure 7, disclosing the amount of saposin in a control population, for a comparison allowing for a determination of deficiency of saposin in a sample population)

wherein the level is an indicator of presence or extent of the disorder in the patient (page 306, right column, second full paragraph.)

As to claim 4, the measured level exceeds a mean level in a control population of individuals not having a lysosomal storage disorder, to indicate presence of the disorder in a patient (page 306, right column, lines 41-42.)

As to claim 7, the measured level is greater than the 95% level in the control population (page 306, right column, lines 41-42.)

As to claim 8, the patient is not known to have a lysosomal storage disorder before the measuring step (page 306, second full paragraph.)

As to claims 13 and 14, the saposin is selected from the group consisting of saposin A, B, C, D, and prosaposin (for example saposin A, page 306, right column, line 41.)

As to claim 15, the measuring step comprises detecting binding between a saposin polypeptide and an antibody (page 306, left column, lines 10-11.)

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As to claim 17, the antibody is immobilized to a solid phase (page 306, right column, , line 18.)

As to claim 18, the lysosomal storage disorder is Niemann-Pick disease (page 306, right column, line 61.)

O'Brien teaches the detection of saposin, and its deficiency or accumulation, in specific tissue and cell samples as an indication of lysosomal storage disorder. However, O'Brien does not specifically teach detection of saposin in whole blood or plasma samples (claims 1-3.)

Sano teaches that saposin is not only found in tissues but is also found in human blood and plasma (see abstract.) It would have been obvious to one of ordinary skill in the art at the time the invention was made to detect saposin in blood or plasma in the O'Brien method of detecting lysosomal storage disease, because Sano teaches that saposin is also found in blood and plasma and Sano teaches measuring levels of saposin in blood. Given the O'Brien teachings in comparing the levels of tissue saposin in a control population and in a sample population with lysosomal storage disorder and given that Sano teaches that saposin is also found in blood or plasma, one of ordinary skill in the art would have reasonable expectation of success for diagnosing or monitoring a lysosomal storage disorder using blood or plasma sample from a patient.

**2.** Claims 5, 6, 9-12, 19, 20 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Brien et al. (1991) Saposin proteins: structure, function, and

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role in human lysosomal disorders, THE FASEB JOURNAL, vol. 5(3), 301-8, in view of Sano et al., "Sphingolipid hydrolase activator proteins and their precursors", Biochemical and biophysical research communications, 165 (3), pp. 1191-7, 1989, and further in view of Dubensky et al., 6,376,236.

The method of O'Brien in view of Sano disclose the invention as claimed (see above). More specifically, O'Brien discloses the correlation between an accumulation of saposin and Gaucher disease in patients, Gaucher disease being a well known lysosomal disease.

However, neither O'Brien nor Sano specifically teach the step of monitoring the progression of the disease (claim 5), the patient undergoing treatment for the lysosomal storage disorder (claim 6), the patient being an infant (claim 9) or fetus (claim 10), (claim 11), nor the step of determining a treatment program (claims 19 and 20), nor the indication of positive treatment (claims 5, 11, 12 and 36.)

Dubensky discloses a method of treating Gaucher's disease (col. 120, lines 33-59.)

As to claims 5, 6, 11, 12 and 36, it would have been obvious to measure the level of the saposin in a second tissue sample from the patient, the first and second samples being obtained at different times; and comparing the levels in the samples to indicate progression of the disease since Dubensky teaches that some lysosomal storage disorders can be responsive to treatment, thus teaching that after treatment, the disorder can be detected by the disclosed method to determine whether the disorder is responsive to the treatment.

Similarly, as to claim 20, it would have been obvious to determine a treatment program based on the measurement since Dubensky teaches that some lysosomal storage disorders can be responsive to treatment, thus teaching that patients can undergo one of these treatments for lysosomal disorder.

Dubensky further teaches that Gaucher's disease affects infants and fetuses, as well as adults, (col. 120, lines 33-59.) It would have been obvious to one of ordinary skill in the art to use the method taught by O'Brien in view of Sano to detect Gaucher's disease in infants and fetuses, since Dubensky teaches that Gaucher's disease affects infants and fetuses, (claims 9 and 10.) As to claim 19, it would have been obvious to one of ordinary skill in the art to inform the patient or a parent or guardian of an infant of the presence of the lysosomal storage disorder, as would be desirable to allow a patient or parent or guardian to permit treatment of the disease.

3. Claim 16 is rejected under 35 U.S.C. 103(a) as being unpatentable over O'Brien, et al. (1991) Saposin proteins: structure, function, and role in human lysosomal disorders, THE FASEB JOURNAL, vol. 5(3), 301-8, in view of Sano et al., "Sphingolipid hydrolase activator proteins and their precursors", Biochemical and biophysical research communications, 165 (3), pp. 1191-7, 1989, as applied to claims 1 and 15, and further in view of Stastny, J., et al. (1992) Production and Characterization of a Monoclonal Antibody to Human Saposin C, HYBRIDOMA, vol. 11, 351-359.

O'Brien in view of Sano disclose the invention substantially as claimed (see above), except for the antibody being a monoclonal antibody.

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Stastny discloses a monoclonal antibody (68-12) that reacts with saposin C. It would have been obvious to use this monoclonal antibody in the method taught by O'Brien in view of Sano in order to detect the level of saposin C because the high specificity of monoclonal antibodies for their corresponding antigen (in this case saposin C) would provide for a more sensitive assay for the detection of saposin C.

### ***Response to Arguments***

Applicant still has not overcome the 112 rejections, as further explained above under the 112 rejections.

Applicant's arguments regarding the 102 and 103 rejections have been considered but are not persuasive. Applicant argues that because O'Brien teaches that the amount of saposin can be variable in different tissues and in different lysosomal storage disorder conditions, one of ordinary skill in the art would not likely be able to predict the alternating levels of saposin in plasma from control and lysosomal storage disorder affected individual. Applicant also argues that Sano does not even mention the levels of saposin from lysosomal storage disorder patients. Applicant asserts that in absence of data indicating any specific saposin protein levels in plasma from Sano, one of ordinary skill in the art could not have predicted the relative levels of saposin proteins in blood needed to diagnose or monitor any lysosomal storage disorder conditions. Applicant also argues that the other cited references do not provide the motivation or suggestion to utilize blood or plasma to diagnose lysosomal storage disorder.

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This is not persuasive because O'Brien teaches determining the amount of saposin in a control population and in a population known to have a lysosomal storage disorder and that a difference in saposin levels are found between the two groups (see page 307, brief description of figure 7, and page 306, lines 10-12 and first sentence of second full paragraph.) Given the O'Brien teachings in comparing the levels of tissue saposin in a control population and in a sample population with lysosomal storage disorder for monitoring lysosomal storage disorder in a patient and given that Sano teaches that saposin is also found in blood or plasma, one of ordinary skill in the art would have reasonable expectation of success for diagnosing or monitoring a lysosomal storage disorder using blood or plasma sample from a patient.

### **Conclusion**

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

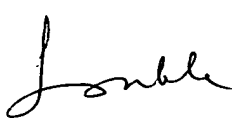
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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ann Y. Lam whose telephone number is 571-272-0822. The examiner can normally be reached on M-Sat 11-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A.L.



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06/26/05